L Number	Hits	Search Text	DB	Time stamp
-	141232	bone marrow or autologous bone marrow	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 10:21
-	2136	(bone marrow or autologous bone marrow) SAME myocardial	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/12/09 10:40
-	317	((bone marrow or autologous bone marrow) SAME myocardial) SAME transplantation	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/12/09 10:40
-	16	fuchs and "autologous bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:30
-	5	RGTA	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:30
-	1741	"cell therapy"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:30
-	2	("cell therapy" same "bone marrow") same transfection	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:31
-	164	"cell therapy" same "bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:31
-	28732	"bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:31
-	3338	"bone marrow" same transfection or "genetic modification"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:32
-	943	"bone marrow" same (transfection of "genetic modification")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:32
-	21413	angiogenic or angiogenesis or neovascularization or "myocardial contractility"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:33
-	6335833	s ("bone marrow" same (transfection of "genetic modification")) same (angiogenic or angiogenesis or neovascularization or "myocardial contractility")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:33
-	7	("bone marrow" same (transfection of "genetic modification")) same (angiogenic or angiogenesis or neovascularization or "myocardial contractility")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:33
-	485	"early attaching cells" or "adhering cells"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:34
-	9	("early attaching cells" or "adhering cells") same (transfection or "genetic modification" or "gene transfer")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/14 18:35
-	28857	"bone marrow" or "autologous bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 11:48

-	905	("bone marrow" or "autologous bone marrow") SAME transfection	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 11:49
-	111	(("bone marrow" or "autologous bone marrow") SAME transfection) SAME "ex vivo"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 11:50
-	4	(("bone marrow" or "autologous bone marrow") SAME transfection) SAME confluent	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 12:00
-	0	(("bone marrow" or "autologous bone marrow") SAME transfection) SAME attach	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 12:00
-	140	("bone marrow" or "autologous bone marrow") SAME attach	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 12:01
-	32	(("bone marrow" or "autologous bone marrow") SAME attach) and transfection	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 12:08
-	56	(("bone marrow" or "autologous bone marrow") SAME attach) and (transfection or transduction)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/20 12:08
-	5773	chiu.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 10:22
-	16	chiu.in. and "bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 11:12
-	635	"ex vivo" NEAR2 expansion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 11:13
-	526	("ex vivo" NEAR2 expansion) and "bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 11:13
-	9	cytokine SAME angio	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 11:20
-	18711	cytokine SAME stimulat$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 11:20
-	295	(("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:14
-	80	((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:05
-	10	((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and MCP	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:09
-	47514	heparin or anticoagulant	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:09
-	33	((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and (heparin or anticoagulant)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:09

-	9	(((((("ex vivo" NEAR2 expansion) and "bone marrow") and (cytokine SAME stimulat$)) and aspirate) and MCP) and (heparin or anticoagulant)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:56
-	49	IL-3 WITH angiogen$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:58
-	52	(IL-3 or IL3) WITH angiogen$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 12:58
-	2	5610056.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:23
-	0	5610056.pn. and heparin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:15
-	0	5610056.pn. and MCP	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:17
-	2	5997860.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:17
-	1	5997860.pn. and "bone marrow"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:17
-	2	5610056.pn. and bone	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:45
-	2	5811297.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:45
-	0	5811297.pn. and MCP	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:45
-	1	5811297.pn. and heparin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:46
-	0	(5811297.pn. and heparin) and stimulate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:46
-	1	(5811297.pn. and heparin) and cytokine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:46
-	1	((5811297.pn. and heparin) and cytokine) and IL-6	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/09/13 13:46

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 FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:12:38 ON 14 SEP 2004
L1        106001 S ANGIOGEN? OR VASCULAROGEN? OR NEOVASCULAR?
L2        117046 S "BONE MARROW" (P) TRANSPLANT?
L3         15232 S "AUTOLOGOUS BONE MARROW"
L4          4589 S "STROMAL CELL" (P) "BONE MARROW"
L5             1 S L1 AND L2 AND L3 AND L4
L6        250991 S HEPARIN OR ANTICOAGULANT
L7         17090 S MCP OR MCP1 OR MCP-1
L8           148 S L6 AND L7
L9             0 S L8 AND L1
L10          344 S L7 AND L1
L11            4 S L10 AND L3
L12            2 DUP REM L11 (2 DUPLICATES REMOVED)
L13            1 S L6 AND L1 AND L3
L14          601 S L6 AND L2
L15           77 S L14 AND L3
L16           59 S L15 NOT PY>=2000
L17           38 DUP REM L16 (21 DUPLICATES REMOVED)
L18          163 S "BLOOD VESSEL" (P) (OCCULSION OR BLOCKAGE OR CLOT)
L19           25 S L18 AND L1
L20           11 S L19 NOT PY>=2000
L21            6 DUP REM L20 (5 DUPLICATES REMOVED)
L22          148 S L7 AND L6
L23            0 S L22 AND L1
L24            0 S L22 AND L3
L25            0 S L22 AND L4
L26           86 S L4 AND L1
L27            0 S L26 AND L18
L28            0 S L4 AND L18
L29           28 S L6 AND L4
L30           14 DUP REM L29 (14 DUPLICATES REMOVED)
L31            6 S L30 NOT PY>=2000
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L5 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:286117 BIOSIS
DOCUMENT NUMBER: PREV200400284874
TITLE: Cardiomyogenic Differentiation and **Neovascularization** by **Autologous Bone Marrow Stromal Cell Transplantation**.
AUTHOR(S): Zhang, Fumin [Reprint Author]; Yang, Zhijian; Ma, Wenzhu; Xu, Qingbin; Zhou, Fang; Zhu, Tiebin; Wang, Nensheng; Chen, Bo; Xu, Zhaoxiang; Ha, Tuanzhu; Li, Chuanfu
CORPORATE SOURCE: Cardiology, Jiangsu Province Hospital; First Affiliated Hospital of Nanjing Medical University, Guanzhu Road, Nanjing, Jiangsu, 210029, China
fmzhang8@public1.ptt.js.cn
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 144.2. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB Induction of **angiogenesis** is fundament for successful therapy in ischemic myocardium. **Bone marrow** cell (BMSC) **transplanted** into ischemic myocardium improves cardiac function. This study evaluated cardiomyogenic differentiation of autologous BMSC and the effect of autologous BMSC on **angiogenesis** in the rat ischemic myocardium. Autologous BMCs were isolated from adult rats, cultured and labeled with Brdu before **transplantation** into ischemic myocardium. Rat myocardial ischemic injury was induced by ligation of left anterior descending (LAD) coronary artery. Brdu labeled BMSCs or culture medium (control) were autologously **transplanted** into ischemic area immediately following LAD ligation (n=6/group). Six weeks after myocardial injury, hearts were harvested and sectioned for immunohistochemistry examination. Anti-myosin heavy chain-β (MHC-β) and anti-connexin43 were utilized to determine the expression of MHC and connexin43 on Brdu labeled cells. Capillary density was counted at five different fields on each slide. Cardiac-like muscle cells stained positive for MHC and connectin43 were observed in the scar tissue of BMSCs **transplanted** hearts. Capillary density in the scar tissue was significantly increased in BMSCs **transplanted** hearts compared to control (14.82 IA 2.44 vs 6.40 IA 1.53). Our results suggest that autologous BMSC **transplantation** can differentiate into cardiac-like muscle cells and significantly induce **angiogenesis** in ventricular scar tissue. .

R 37 OF 38 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 85189779 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3887329
TITLE: [Venous occlusive disease of the liver and **autologous bone marrow transplantation**. Preventive role for **heparin**?].
Maladie veino-occlusive du foie et autogreffe de moelle osseuse. Role preventif de l'heparine?.
AUTHOR: Cahn J Y; Flesch M; Plouvier E; Herve P; Rozenbaum A
SOURCE: Nouvelle revue francaise d'hematologie, (1985) 27 (1) 27-8.
Journal code: 7909092.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198506
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850618

AB The pathogenesis of veno-occlusive disease (VOD) of the liver remains unclear. In a retrospective study we reviewed 63 patients treated with high dose conditioning regimens followed by **autologous bone marrow transplant**. All patients were given low dose **heparin** (1 mg/kg). Only one patient developed VOD when **heparin** was stopped. We think that low dose **heparin** seems an interesting proposal for an randomized study to prevent VOD.

migration of pre-endocardial angioblasts and that the pattern of the cranioventral vasculature forms independent of the source of angioblasts. Transplant experiments showed that the origin for endocardial angioblasts lies in mesodermal tissue just anterior to Henson's node, that these cells undergo directed migration to the pericardial area, and that angioblasts are pluripotent with the ability to form different blood vessels. The transplant studies also showed that the embryonic mesoderm may contribute to extraembryonic blood vessels on the embryonic yolksac. These results support the hypothesis that embryonic blood vessels may develop by either the vasculogenesis or by the **angiogenesis** mechanism, and show that the endocardium of the primitive heart tube forms by vasculogenesis.

L21 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1990:161050 BIOSIS
DOCUMENT NUMBER: PREV199089088468; BA89:88468
TITLE: BIOCHEMICAL ANALYSIS OF SERUM PROTEINS FROM EALES' PATIENTS.
AUTHOR(S): RENGARAJAN K [Reprint author]; MUTHUKKARUPPAN V R; NAMPERUMALSAMY P
CORPORATE SOURCE: DEP IMMUNOL SCH BIOLOGICAL SCI, MADURAI KAMARAJ UNIV, MADURAI-625 021, INDIA
SOURCE: Current Eye Research, (1989) Vol. 8, No. 12, pp. 1259-1270. CODEN: CEYRDM. ISSN: 0271-3683.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 27 Mar 1990
Last Updated on STN: 27 Mar 1990
AB In the present study attempt has been made to identify the possible factor(s) which are responsible for Eales' disease. The serum of Eales' patients and that of age and sex matched healthy controls did not differ in their total protein concentration. Sodium dodecylsulphate polyacrylamide gel electrophoresis (SDS-PAGE) analysis did not reveal any difference between the two groups. However, analysis of the serum samples with isoelectric focusing showed the presence of two unique proteins with pI of 5.5 and 5.9 in Eales' patients. Further two dimensional SDS-PAGE analysis indicated the presence of a distinct protein spot with a pI of 5.9 and a molecular weight around 23 KD in the serum of Eales' patients. This 23 KD protein has been partially purified and found to be anionic in nature. Antisera to this partially purified protein have been raised and tested. The implication of this finding is discussed in relation to the aetiology of Eales' disease.

L21 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 89150279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2465781
TITLE: Pathogenesis of tumor stroma generation: a critical role for leaky blood vessels and fibrin deposition.
AUTHOR: Nagy J A; Brown L F; Senger D R; Lanir N; Van de Water L; Dvorak A M; Dvorak H F
CORPORATE SOURCE: Department of Pathology, Beth Israel Hospital, Boston, MA 02215.
CONTRACT NUMBER: CA 28471 (NCI)
CA 40624 (NCI)
CA 43967 (NCI)
+
SOURCE: Biochimica et biophysica acta, (1989 Feb) 948 (3) 305-26.
Ref: 131
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890410

AB Tumor stroma formation results from the interaction of tumor cells and their products with the host and certain of its normal defense mechanisms, particularly the clotting and fibrinolytic systems. It is a process in which tumor cells render local venules and veins hyperpermeable with the result that fibrinogen and other proteins extravasate and **clot**, forming an extravascular crosslinked fibrin gel. Coagulation is mediated by an interaction between extravasated plasma clotting factors and tumor-associated and perhaps other tissue procoagulants. Parallel activation of the fibrinolytic system leads to substantial fibrin turnover, but fibrin nonetheless accumulates in amounts, variable from tumor to tumor, that are sufficient to provide a provisional stroma. This provisional stroma imposes on tumor cells a structure that persists even as tumor cells multiply and as the fibrin provisional stroma is replaced by mature connective tissue. The provisional fibrin stroma also serves to regulate the influx of macrophages, and perhaps other inflammatory cells, but at the same time, and in ways that are not fully understood, facilitates the inward migration of new blood vessels and fibroblasts, integral components of mature tumor stroma. Ascites tumors differ from solid tumors in that fibrin gel is not ordinarily deposited in body cavities and, as a result, there is no provisional stroma to impose an initial structure. Tumor stroma generation resembles the process of wound healing in many respects. However, it differs in the mechanism of its initiation, and in the apparent lack of a role for platelets. It also differs fundamentally in that invading tumor cells continually render new vessels hyperpermeable to plasma, thus perpetuating the cycle of extravascular fibrin deposition. In this sense, tumors behave as wounds that do not heal. Largely neglected in this review has been discussion of the numerous cytokines, mitogens, and growth factors that are widely believed to play important roles in tumor **angiogenesis** and wound healing; i.e., PDGF, FGF, EGF, TGF alpha, TGF beta, TNF, interferons, etc. This omission has been intentional, and for two reasons. First, these cytokines have already received considerable attention [100,123-128]. Second, it is not yet clear how closely the actions of these molecules, as described in vitro, relate to their functions in vivo. At present we are deluged with a surfeit of factors that have the capacity to induce new **blood vessel** formation in **angiogenesis** assays; these factors include not only peptides but lipids and even ions [126,129-131].(ABSTRACT TRUNCATED AT 400 WORDS)

L21 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 88099537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3321439
TITLE: Endothelial cell growth factors and the vessel wall.
AUTHOR: Joseph-Silverstein J; Rifkin D B
CORPORATE SOURCE: Department of Cell Biology, New York University Medical Center, NY 10016.
SOURCE: Seminars in thrombosis and hemostasis, (1987 Oct) 13 (4) 504-13. Ref: 84
Journal code: 0431155. ISSN: 0094-6176.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 19900305

Last Updated on STN: 19900305
Entered Medline: 19880209

AB The role of endothelial cell growth factors in the maintenance of the **blood vessel** wall is, as we have described here, much more complex than merely stimulating the mitogenesis of endothelial cells. The FGFs are capable of eliciting an array of responses in endothelial cells, some, or all, of which are important for **neovascularization** and the control of **clot** dissolution. These endothelial cell responses include protease elaboration, chemotaxis, and mitogenesis. That these growth factors seem neither to be constitutively released into the medium of cultured cells that synthesize bFGF, nor released into the bloodstream in vivo suggests that the temporal and local control of **neovascularization** may involve the regulation of growth factor release from cells such as endothelial cells, fibroblasts, and macrophages. Although there is no known example of this for bFGF, it is well known that both thrombin and Factor Xa stimulate the release of a mitogenic protein from endothelial cells and that low oxygen tension stimulates the release of macrophage-derived **angiogenesis** factor. In addition, both TGF beta and heparin alone appear to play a role in wound healing and vessel wall maintenance. The work of Roberts et al suggests that TGF beta is not only **angiogenic**, but also stimulates the growth of fibrotic tissue as well. Studies on mast cells demonstrated that released heparin is chemotactic for endothelial cells and can potentiate tumor **angiogenesis**. An attractive hypothesis is that these molecules not only act as FGF potentiators or inhibitors but that they also may exert their **angiogenic** effects by inducing FGF release from cells. Perhaps **angiogenin**, an **angiogenic** molecule with no mitogenic activity, works in this way. However, no evidence as yet exists concerning this point. A second level of control of **neovascularization** may involve the interaction of FGF with other molecules released into the same microenvironment. For example, thrombin and TGF beta released from platelets, as well as heparin released from mast cells, have all been demonstrated to affect bFGF activity in vitro and may act as modifiers of FGF activity in vivo. Since bFGF can modulate fibrinolytic activity, one could imagine that its release into a wound region of the vasculature could have detrimental effects on **clot** formation and subsequent wound healing. Thus, the transient inhibition of bFGF activity by TGF beta would allow **clot** formation before the induction of **neovascularization** by bFGF, TGF beta thereby playing a role in the regulation of the sequence in which events occur. (ABSTRACT TRUNCATED AT 400 WORDS)

NSWER 1 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999180642 EMBASE
TITLE: Technology evaluation: Gene therapy (FGF-5), Vical.
AUTHOR: Li K.; Stewart D.J.; Ward H.J.
CORPORATE SOURCE: K. Li, Hypertension/Vascular Biol. Lab., Division of Nephrology/Hypertension, King/Drew Medical Center, 12021 South Wilmington St, Los Angeles, CA 90059, United States. kaili34@yahoo.com
SOURCE: Current Opinion in Molecular Therapeutics, (1999) 1/2 (260-265).
Refs: 73
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Vical, in collaboration with Merck, is developing gene-based therapies, including its 'naked DNA', for the potential treatment of ischemic heart disease. Vical has obtained preclinical data in animal models showing that a gene for a potent growth factor, FGF-5, can be delivered and expressed in coronary arteries stimulating the formation of new blood vessels. This new **blood vessel** formation may provide supplemental blood flow and necessary cardiac tissue oxygenation in areas of the heart where atherosclerotic blockages are present. Vical anticipates that its FGF-5 gene-based product would be used in conjunction with balloon angioplasty to stimulate new **blood vessel** formation at the site of the **blockage**. A series of experiments have been conducted in rats, whereby genes encoding FGF-5 were injected directly into rat heart muscle. The DNA was absorbed and the FGF-5 protein was expressed by cardiac myocytes. Active FGF-5 was released into the extracellular spaces of the heart muscle cells and new blood vessels formed throughout the local area. Quantitative measurements of **blood vessel** formation indicated that capillary density increased significantly in the hearts of treated rats compared to untreated controls. Further studies are underway to evaluate the persistence of new blood vessels following FGF-5 gene injection, and measurements will be made to assess the extent of improved blood flow in the affected region [177118]. In December 1996, the US patent office issued patent number US-05580859, covering Vical's naked DNA technology [227199].

L21 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1998244865 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9578571
TITLE: Structural features that determine the enzymatic potency and specificity of human **angiogenin**: threonine-80 and residues 58-70 and 116-123.
AUTHOR: Shapiro R
CORPORATE SOURCE: Center for Biochemical and Biophysical Sciences and Medicine, Boston, Massachusetts 02115, USA.. shapiro@ferret.med.harvard.edu
CONTRACT NUMBER: HL52096 (NHLBI)
SOURCE: Biochemistry, (1998 May 12) 37 (19) 6847-56.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806

ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980604

AB Human **angiogenin** (Ang), a homologue of bovine pancreatic ribonuclease A (RNase A), is a potent inducer of **blood vessel** formation. It exerts a ribonucleolytic activity that is 10(5)-10(6)-fold lower than that of RNase A but nonetheless essential for biological action. Previous studies revealed some of the structural features of Ang that underlie its catalytic inefficiency: Gln-117 blocks the space corresponding to the pyrimidine binding site of RNase A and Ang lacks the disulfide loop 65-72 that forms most of the purine binding site of RNase A. Additional features have now been identified by mutagenesis and kinetics. Thr-80, which hydrogen-bonds to the pyrimidine-binding residue Thr-44, plays an important part in attenuating activity and in determining pyrimidine specificity: mutation to Ala increases activity toward cytidylyl substrates by 11-15-fold but has only a minimal effect on cleavage of uridylyl substrates. The properties of T44A/T80A and Q117A/T80A double mutants demonstrate that these changes are mediated by Thr-44 and are largely independent of the **blockage** by Gln-117. The side chain of Ser-118 also suppresses enzymatic activity: S118A is 5-7-fold more effective than Ang. This increase appears to reflect the loss of a hydrogen bond with Asp-116 that helps to orient Gln-117. The effects of deleting residues 119-123 suggest that main-chain atoms of the C-terminal 3(10) helix make a small further contribution. Finally, the significance of the absence of the RNase A loop 65-72 from Ang has been investigated by reexamining the earlier derivative ARH-I (in which Ang residues 58-70 have been replaced by residues 59-73 of RNase) and generating new derivatives of this hybrid protein. The results suggest that the RNase A segment of ARH-I not only provides more effective purine recognition but also counteracts the deleterious effects of Gln-117 and Thr-80 on the pyrimidine site.

L21 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 92109303 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1763820
TITLE: Endothelial cell origin and migration in embryonic heart and cranial blood vessel development.
AUTHOR: Coffin J D; Poole T J
CORPORATE SOURCE: Department of Anatomy and Cell Biology, SUNY Health Science Center, Syracuse 13210.
SOURCE: Anatomical record, (1991 Nov) 231 (3) 383-95.
Journal code: 0370540. ISSN: 0003-276X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920302
Last Updated on STN: 19920302
Entered Medline: 19920207

AB Using the QH-1 monoclonal antibody as a marker for quail endothelium, **blockage** and transplant experiments were carried out to construct fate maps for the embryonic endocardium, to determine whether preendocardial angioblasts are migratory, and, if these cells are migratory, to outline the pathways that they use for directed migration in embryonic **blood vessel** development. Recent descriptive studies using QH-1 to make immunofluorescent whole mounts have described a sequence of events leading to the establishment of the embryonic heart tube. These reports suggest that the pattern for the endocardium and cranial vasculature is established by migrating angioblasts that form vascular cords which mature into blood vessels. **Blockage** experiments showed that the ventrolateral edge of the anterior intestinal portal serves as a substrate for the directed

NSWER 1 OF 6 MEDLINE on STN
ACCESSION NUMBER: 97427278 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9282310
TITLE: Enhanced growth of canine **bone marrow stromal cell** cultures in the presence of acidic fibroblast growth factor and **heparin**.
AUTHOR: Emami S; Merrill W; Cherington V; Chiang G G; Kirchgesser M; Appel J M; Hansen M; Levine P H; Greenberger J S; Hurwitz D R
CORPORATE SOURCE: ALG Company, Marlboro, Massachusetts 01752, USA.
SOURCE: In vitro cellular & developmental biology. Animal, (1997 Jul-Aug) 33 (7) 503-11.
Journal code: 9418515. ISSN: 1071-2690.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971028

AB The ex vivo establishment, expansion, transduction, and reintroduction of autologous **bone marrow** stromal cells offers a potential efficacious system for somatic cell gene therapy. It is likely that any ex vivo system will require the use of large numbers of cells which express high levels of transgene products. We present a method for routine expansion of canine **bone marrow** stromal cells, established from initial 10-20 ml marrow aspirates, to greater than 10(9) cells. This high level expansion of cell cultures uses the stimulatory effect of acidic fibroblast growth factor (aFGF) and **heparin**. In the absence of these factors, **stromal cell** cultures grow actively for only 1 to 2 passages, become flattened in morphology, and expand to only 10(8) cells. In the presence of **heparin** (5 U/ml), aFGF exerts its effect over a wide range of concentrations (0.1-10 ng/ml) in a dose-dependent manner. The stimulatory effect is dependent on the presence of both aFGF and **heparin**. Immunocytochemical and cytochemical analyses phenotypically characterize these stromal cells as **bone marrow** stromal myofibroblasts. Stromal cells grown in the presence of aFGF and **heparin** grow actively and maintain a fibroblast-like morphology for a number of passages, transduce efficiently with a human growth hormone (hGH) expression vector, and express and secrete high levels of hGH. Human marrow stromal cells were also established and expanded by the same culture method. This culture method should be of great value in somatic cell gene therapy for the delivery of secreted gene products to the plasma of large mammals.

L31 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 93372339 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8364196
TITLE: A novel 37-Kd adhesive membrane protein from cloned murine bone marrow stromal cells and cloned murine hematopoietic progenitor cells.
AUTHOR: Shiota Y; Wilson J G; Harjes K; Zanjani E D; Tavassoli M
CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Jackson, MS 39216.
CONTRACT NUMBER: DK30142 (NIDDK)
HL40722 (NHLBI)
HL46556 (NHLBI)
+
SOURCE: Blood, (1993 Sep 1) 82 (5) 1436-44.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931022
Last Updated on STN: 19931022
Entered Medline: 19931005

AB The adhesion of hematopoietic progenitor cells to **bone marrow** stromal cells is critical to hematopoiesis and involves multiple effector molecules. **Stromal cell** molecules that participate in this interaction were sought by analyzing the detergent-soluble membrane proteins of GBI/6 stromal cells that could be adsorbed by intact FDCP-1 progenitor cells. A single-chain protein from GBI/6 cells having an apparent molecular weight of 37 Kd was selectively adsorbed by FDCP-1 cells. This protein, designated p37, could be surface-radiolabeled and thus appeared to be exposed on the cell membrane. An apparently identical 37-Kd protein was expressed by three **stromal cell** lines, by Swiss 3T3 fibroblastic cells, and by FDCP-1 and FDCP-2 progenitor cells. p37 was selectively adsorbed from membrane lysates by a variety of murine hematopoietic cells, including erythrocytes, but not by human erythrocytes. Binding of p37 to cells was calcium-dependent, and was not affected by inhibitors of the hematopoietic homing receptor or the cell-binding or **heparin**-binding functions of fibronectin. It is proposed that p37 may be a novel adhesive molecule expressed on the surface of a variety of hematopoietic cells that could participate in both homotypic and heterotypic interactions of stromal and progenitor cells.

L31 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 93152832 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8427958
TITLE: Basic fibroblast growth factor expression in human bone marrow and peripheral blood cells.
AUTHOR: Brunner G; Nguyen H; Gabrilove J; Rifkin D B; Wilson E L
CORPORATE SOURCE: Department of Cell Biology, New York University Medical Center, NY 10016.
CONTRACT NUMBER: CA 20194 (NCI)
CA 34282 (NCI)
CA 49419 (NCI)
SOURCE: Blood, (1993 Feb 1) 81 (3) 631-8.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930326
Last Updated on STN: 19930326
Entered Medline: 19930310

AB We have shown previously that basic fibroblast growth factor (bFGF) is a mitogen for human **bone marrow** (BM) stromal cells and that bFGF stimulates myelopoiesis in primary BM cultures. In this article, we demonstrate the presence of bFGF in two cell lineages in human BM and peripheral blood as well as the deposition of bFGF into the extracellular matrix of BM **stromal cell** cultures. In immunofluorescence experiments on BM and peripheral blood smears, megakaryocytes and platelets stained strongly for bFGF, whereas weaker staining was observed in immature and mature cells of the granulocyte series. The presence of bFGF in platelets was confirmed by enzyme-linked immunosorbent assay as well as by immunoprecipitation followed by immunoblotting. bFGF was synthesized by BM **stromal cell** cultures and was found either cell associated or localized in the nucleus and the nucleoli, and its location was dependent on the fixation procedure used. Addition of exogenous bFGF to stromal cells showed the presence of

extracellular binding molecules for this cytokine. bFGF could be released from these sites by soluble **heparin** or phosphatidylinositol-specific phospholipase C. This study supports the role of bFGF as a **stromal cell** mitogen and stimulator of myelopoiesis.
The data indicate that the stromal cells produce bFGF and that their extracellular matrix can serve as a reservoir for this growth factor. In addition, the results suggest a possible involvement of bFGF in platelet function as well as in megakaryocytopoiesis.

L31 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 91319212 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1861722
TITLE: Fibronectin and VLA-4 in haematopoietic stem cell-microenvironment interactions.
AUTHOR: Williams D A; Rios M; Stephens C; Patel V P
CORPORATE SOURCE: Howard Hughes Medical Institute, Boston, Massachusetts.
SOURCE: Nature, (1991 Aug 1) 352 (6334) 438-41.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19910922
Last Updated on STN: 19910922
Entered Medline: 19910905

AB The self-renewal and differentiation of haematopoietic stem cells occurs in vivo and in vitro in direct contact with cells making up the haematopoietic microenvironment. In this study we used adhesive ligands and blocking antibodies to identify **stromal cell** -derived extracellular matrix proteins involved in promoting attachment of murine haematopoietic stem cells. Here we report that day-12 colony-forming-unit spleen (CFU-S12)5 cells and reconstituting haematopoietic stem cells attach to the C-terminal, **heparin** -binding fragment of fibronectin by recognizing the CS-1 peptide of the alternatively spliced non-type III connecting segment (IIICS) of human plasma fibronectin. Furthermore, CFU-S12 stem cells express the alpha 4 subunit of the VLA-4 integrin receptor, which is known to be a receptor for the CS-1 sequence, and monoclonal antibodies against the integrin alpha 4 subunit of VLA-4 block adhesion of CFU-S12 stem cells to plates coated with the C-terminal fibronectin fragment. Finally, polyclonal antibodies against the integrin beta 1 subunit of VLA-4 inhibit the formation of CFU-S12-derived spleen colonies and medullary haematopoiesis in vivo following intravenous infusion of antibody-treated **bone marrow** cells.

L31 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 91201809 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1901881
TITLE: Role of glycosaminoglycans in the regulation of T cell proliferation induced by thymic stroma-derived T cell growth factor.
AUTHOR: Kimura K; Matsubara H; Sogoh S; Kita Y; Sakata T; Nishitani Y; Watanabe S; Hamaoka T; Fujiwara H
CORPORATE SOURCE: Biomedical Research Center, Osaka University Medical School, Japan.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1991 Apr 15) 146 (8) 2618-24.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910607
Last Updated on STN: 19910607
Entered Medline: 19910521

AB The present study investigates the regulatory effects of glycosaminoglycans such as **heparin** and heparan sulfate on T cell proliferation induced by thymic **stromal cell** monolayer or its derived T cell growth factor (TCGF). A thymic **stromal cell** clone (MRL104.8a) supported the growth of Ag-specific, IL-2-dependent Th cell clone (9-16) in the absence of Ag and IL-2 by producing a unique TCGF designated as thymic stroma-derived T cell growth factor (TSTGF). The addition of **heparin** to cultures in which the growth of 9-16 Th cells was otherwise stimulated by the MRL104.8a monolayer or a semipurified sample of the TSTGF resulted in **heparin** dose-dependent inhibition of 9-16 Th proliferation. The dose of **heparin** required for inducing 50% reduction of TSTGF-induced proliferation of Th at a given cell number was found to be proportional to the magnitude of the TSTGF added to cultures, suggesting that **heparin** exerted its inhibitory effect by binding to the TSTGF rather than by acting on Th cells. A similar growth-inhibiting effect of **heparin** was observed in IL-7-dependent proliferation of pre-B cell line or Th, but not in IL-2-dependent T cell proliferation or IL-3-dependent myeloid cell proliferation. A strong affinity of TSTGF and IL-7 for **heparin** was confirmed by the fact that both TSTGF and IL-7 adhered to columns of **heparin**-agarose and were eluted by salt. When various glycosaminoglycans were tested for the **heparin**-like Th growth-regulatory capacity, heparan sulfate exhibited Th growth-inhibiting ability comparable to that observed for **heparin**. These results indicate that the activity of thymic and/or **bone marrow** stroma-derived lymphocyte growth factor (TSTGF/IL-7) but not of Th-producing TCGF (IL-2) is negatively regulated by **heparin** or heparan sulfate, which would represent major glycosaminoglycans in the extra-cellular matrix of stromal cells.

L31 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 91058767 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2245044
TITLE: Long-term culture of human bone marrow stromal cells in the presence of basic fibroblast growth factor.
AUTHOR: Oliver L J; Rifkin D B; Gabrilove J; Hannocks M J; Wilson E L
CORPORATE SOURCE: Department of Cell Biology, New York University Medical Center, New York 10016.
CONTRACT NUMBER: CA 23753 (NCI)
CA 49419 (NCI)
SOURCE: Growth factors (Chur, Switzerland), (1990) 3 (3) 231-6.
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910222
Last Updated on STN: 19970203
Entered Medline: 19910108

AB Basic fibroblast growth factor (bFGF) is a potent mitogen for human **bone marrow** stromal cells. Normally, large numbers of human **bone marrow** stromal cells are difficult to obtain. However, nanogram/ml concentrations of bFGF stimulate the growth of passaged **bone marrow** stromal cells both in media formulated for optimal growth of stromal cells and in a simple mixture of RPMI-1640 and 10% fetal calf serum facilitating the successive expansion of stromal cells through multiple passages. bFGF also greatly accelerates

the formation of a primary **stromal cell** layer following inoculation of newly harvested **bone marrow** cells into dishes. In the presence of bFGF, the stromal cells attain high densities, lose their contact inhibition and grow in multilayered sheets. **Heparin** greatly potentiates the stimulatory effect of low concentrations of bFGF. The effects of bFGF are fully reversible: cells cultured in the presence of this factor for multiple passages revert to normal growth rates following trypsinization and subculture. A short (4 h) exposure of the cells to bFGF elicits profound growth stimulation. This supports the hypothesis that this factor binds to glycosaminoglycans in the cell matrix which act as a storage reservoir for this cytokine.

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